Claims

[c1] 1. A process for the solid phase synthesis of peptides, which comprises:

(a) deprotecting a first amino acid linked to a solid phase resin by removing protective first chemical groups;

(b) activating chemical groups on a second amino acid to prepare the second amino acid for coupling with the first amino acid;

(c) coupling the activated second amino acid to the deprotected first amino acid to form a peptide from the first and second amino acids; and

(e) applying microwave energy to accelerate the deprotecting, activating, and coupling cycle.

[c2] 2. A process according to Claim 1 comprising cleaving the peptide from the solid phase resin while applying microwave energy to accelerate the cleaving step.

[c3] 3. A peptide synthesis process according to Claim 1, comprising repeating the deprotecting, activating, and coupling cycle to add third and successive acids to form a peptide of a desired sequence.

[c4] 4. A peptide synthesis process according to Claim 1, comprising successively deprotecting, activating, and coupling a plurality of amino acids into a peptide in a single vessel

without removing the peptide-linked resin from the vessel between cycles.

[c5] 5. A peptide synthesis process according to Claim 1, comprising proactively cooling the vessel and its contents during the application of microwave energy to thereby prevent undesired degradation of the peptide or acids by limiting heat accumulation that would otherwise result from the application of the microwave energy.

[c6] 6. A peptide synthesis process according to Claim 1, wherein the deprotecting step comprises deprotecting the alpha-amino group of the amino acid.

[c7] 7. A peptide synthesis process according to Claim 1, further comprising deprotecting side chains on the amino acids of the peptide under microwave irradiation.

[c8] 8. A peptide synthesis process according to Claim 1, wherein the activating step comprises activating the alpha-carboxyl group of the second amino acid.

[c9] 9. A peptide synthesis process according to Claim 1, wherein the step of applying the microwave energy comprises limiting the application of microwave energy to relatively short time intervals to thereby prevent undesired degradation of the peptide or acids by limiting heat accumulation that could be encouraged by the continuous application of the microwave

energy.

[c10] 10. A peptide synthesis process according to Claim 1 further comprising activating and coupling using an *in situ* method and a composition selected from the group consisting of phosphorium activators, uronium activators, HATU, HBTU, PyBOP, PyAOP, and HOBT.

[c11] 11. A peptide synthesis process according to Claim 1 comprising monitoring the temperature of the vessel and moderating the applied power based upon the monitored temperature.

[c12] 12. A peptide synthesis process according to Claim 1 comprising moderating the applied power based on the status of the reaction.

[c13] 13. An apparatus for the accelerated synthesis of peptides by the solid phase method, said vessel system comprising:
a reaction cell that is transparent to microwave radiation;
a passageway for adding liquids to said reaction cell;
a passageway for removing liquids but not solids from said reaction cell;
a microwave cavity for holding said cell; and
a microwave source in wave communication with said cavity.

[c14] 14. A vessel system for the accelerated synthesis of peptides by the solid phase method, said vessel system comprising:

a reaction cell that is transparent to microwave radiation;
a first passageway in fluid communication with said cell for transferring solid phase resin between a resin source external to said cell and said cell;
a second passageway in fluid communication between at least one amino acid source and said cell for adding amino acids to said cell;
a third passageway in gaseous communication with an inert gas source and with a vent for applying gas pressure to and releasing gas pressure from said cell so that the controlled flow of gases to and from said cell can be used to add and remove fluids and flowing solids to and from said cell.

[c15] 15. A peptide synthesis vessel system according to Claim 14 comprising a processor and control system for controlling said passageways to sequentially add acids to the vessel and peptide and to transfer completed peptides from said vessel to a peptide reservoir.

[c16] 16. A peptide synthesis vessel system according to Claim 15 comprising means for rinsing said vessel with solvent from an external solvent source and thereafter sequentially adding acids to said vessel to form a subsequent peptide in said same vessel.

[c17] 17. A peptide synthesis vessel system according to Claim 14, further comprising a filter in said second passageway for

preventing solid phase resin from entering said second passageway from said cell.

[c18] 18. A peptide synthesis vessel system according to Claim 14, further comprising a fourth passageway in fluid communication between an external solvent source and said cell for flushing said cell with solvent.

[c19] 19. A peptide synthesis vessel system according to Claim 18, wherein said fourth passageway terminates within said cell with a spray head mechanism.

[c20] 20. A peptide synthesis vessel system according to Claim 14, wherein said inert gas source is selected from the group consisting of pressurized nitrogen gas and pressurized argon gas.

[c21] 21. A peptide synthesis vessel system according to Claim 20, comprising a regulator for controlling the pressurized gas.

[c22] 22. A peptide synthesis vessel system according to Claim 14, comprising a valve system for controlling fluid communication in said first passageway.

[c23] 23. A peptide synthesis vessel system according to Claim 14, comprising a valve system for controlling fluid communication in said second passageway.

[c24] 24. A peptide synthesis vessel system according to Claim 14,

comprising a valve system for controlling gaseous communication in said third passageway.

[c25] 25. A peptide synthesis vessel system according to Claim 18, comprising a valve system for controlling fluid communication in said fourth passageway.

[c26] 26. A peptide synthesis vessel system according to Claim 14, wherein said first and said second passageways are in further fluid communication with respective external solvent sources.

[c27] 27. A peptide synthesis vessel system according to Claim 18, wherein said fourth passageway is in further fluid communication with an external solvent source.

[c28] 28. A peptide synthesis vessel system according to Claim 14, comprising a resin reservoir in fluid communication with said first passageway for depositing solid phase resin in said cell.

[c29] 29. A peptide synthesis vessel system according to Claim 28, comprising a resin reservoir group.

[c30] 30. A peptide synthesis vessel system according to Claim 29 wherein said resin reservoir group comprises between one and twelve reservoirs.

[c31] 31. A peptide synthesis vessel system according to Claim 14, comprising an amino acid reservoir in fluid communication with said second passageway for depositing the desired amino

acid in said cell.

[c32] 32. A peptide synthesis vessel system according to Claim 31 comprising an amino acid reservoir group.

[c33] 33. A peptide synthesis vessel system according to Claim 32 wherein said amino acid reservoir group comprises between one and twenty reservoirs.

[c34] 34. A peptide synthesis vessel system according to Claim 14, comprising a peptide reservoir in fluid communication with said second passageway for depositing the completed peptide in said peptide reservoir.

[c35] 35. A peptide synthesis vessel system according to Claim 34, comprising a peptide reservoir group.

[c36] 36. A peptide synthesis vessel system according to Claim 35 wherein said peptide reservoir group comprises between one and twelve reservoirs.

[c37] 37. A peptide synthesis vessel system according to Claim 14, comprising a liquid waste container in fluid communication with said second passageway for depositing solvent waste therein.

[c38] 38. A peptide synthesis vessel system according to Claim 14, comprising a resin waste container in fluid communication with said first passageway for depositing resin waste therein.

[c39] 39. A peptide synthesis vessel system according to Claim 14, comprising an amino acid reservoir group and a peptide reservoir group, each of which is in fluid communication with said second passageway and with one or more valves for controlling fluid communication between said amino acid and peptide reservoir groups and said cell.

[c40] 40. A peptide synthesis vessel system according to Claim 14, comprising a dedicated cleaving solution reservoir and with a dedicated passageway in fluid communication with said cleaving solution reservoir and said cell.

[c41] 41. A peptide synthesis vessel system according to Claim 18 comprising a valving mechanism in fluid communication with said second, said third, and said fourth passageways that defines a flow path selected from the group consisting of sample loops and fluid bypass circuits.

[c42] 42. A peptide synthesis vessel system according to Claim 41 further comprising liquid sensors for determining liquid volume in said sample loop and said cell.

[c43] 43. A peptide synthesis vessel system according to Claim 14, comprising between one and twenty sources for common amino acids or acid derivatives.

[c44] 44. A peptide synthesis vessel system according to Claim 14 comprising a microwave source and a cavity for said vessel

with said source being in wave communication with said cavity.

[c45] 45. A peptide synthesis instrument according to Claim 44, further comprising a waveguide for wave communication between said microwave source and said cavity.

[c46] 46. A peptide synthesis vessel system according to Claim 14 comprising an infrared temperature sensor capable of measuring and positioned to measure the infrared radiation emitted by the contents of said cell in said cavity without contacting the contents of said cell.

[c47] 47. A peptide synthesis vessel system according to Claim 46 wherein said temperature sensor comprises an infrared photosensor that specifically measures the temperature of the contents of said cell.

[c48] 48. A peptide synthesis vessel system according to Claim 14, further comprising means for simultaneously cooling said cell during the application of microwave radiation.

[c49] 49. A peptide synthesis vessel system according to Claim 48, further comprising means for simultaneously cooling said cell by circulating air upon said reaction cell.

[c50] 50. A peptide synthesis vessel system according to Claim 14, wherein said cooling means operates between applications of

microwave radiation for at least the deprotecting, activating, and coupling steps.

[c51] 51. A process for accelerating the solid phase synthesis of peptides, and comprising:
deprotecting a protected first amino acid linked to a solid phase resin by admixing the protected linked acid with a deprotecting solution in a microwave transparent vessel while irradiating the admixed acid and solution with microwaves;
activating a second amino acid by adding the second acid and an activating solution to the same vessel while irradiating the vessel with microwaves;
coupling the second amino acid to the first acid while irradiating the composition in the same vessel with microwaves; and
cleaving the linked peptide from the solid phase resin by admixing the linked peptide with a cleaving composition in the same vessel while irradiating the composition with microwaves.

[c52] 52. A peptide synthesis process according to Claim 51 comprising cooling the vessel during any one or more of the deprotecting, activating, coupling and cleaving steps to prevent heat accumulation from the microwave energy from degrading the solid phase support or the peptide.

[c53] 53. A peptide synthesis process according to Claim 51,

comprising cyclically repeating the steps of deprotecting, activating, and coupling for three or more amino acids in succession to thereby synthesize a desired peptide.

[c54] 54. A peptide synthesis process according to Claim 51, comprising carrying out said successive deprotecting, activating, coupling, and cleaving steps in the single reaction vessel without removing the peptide from the solid phase resin or from the vessel between cycles.

[c55] 55. A peptide synthesis process according to Claim 51 further comprising agitating the admixture with nitrogen gas during one or more of the deprotecting, activating, coupling, and cleaving steps.

[c56] 56. A peptide synthesis process according to Claim 51 comprising deprotecting the alpha-amino group of the amino acid.

[c57] 57. A peptide synthesis process according to Claim 56 comprising deprotecting the alpha-amino group of the amino acid with a composition suitable for removing protective chemicals selected from the group consisting of N Î±-9-fluorenylmethyloxycarbonyl (Fmoc) and NÎ±-t-butoxycarbonyl (Boc).

[c58] 58. A peptide synthesis process according to Claim 51 comprising deprotecting the side chain of the amino acid.

[c59] 59. A peptide synthesis process according to Claim 58 comprising deprotecting the side chain of the amino acid with a composition suitable for removing t-butyl-based side chain protecting groups.

[c60] 60. A peptide synthesis process according to Claim 51 further comprising activating and coupling the second amino acid *in situ* using a carbodiimide-type coupling reagent.

[c61] 61. A peptide synthesis process according to Claim 51 further comprising a cleaving composition of trifluoroacetic acid and containing a plurality of scavenging agents to quench the reactive carbonium ions that originate from the protective groups and linkers.